

role of genetic factor is a perspective direction of oncogenecology. The clinical-genealogical analysis of thousands of genealogies of patients with cancer of female reproductive organs, allowed H.Linch et al to unify the clinical-genealogical criteria which allow to distinguish between inherited and sporadic tumors. The study goal was establishment of features and patterns of distribution of tumors in families of patients with ovarian and endometrial cancer. The clinical-genealogical analysis of 520 patients with ovarian cancer and 482 patients with endometrial cancer in Chernivtsi region was conducted. The analysis revealed that the most common malignancies in families of these patients were tumors of female reproductive organs (ovarian, endometrial and breast cancer), gut (stomach, colon), lungs, prostate etc. Among 520 genealogies of patients with ovarian cancer and 482 genealogies of patients with endometrial cancer we selected 103 genealogies in which malignant tumors of female reproductive sphere were twice more common, which is a clinical-genealogical criterion of family cancer of female reproductive sphere. We analyzed the spectrum of family aggregation of cancer of different anatomic localizations in these 103 genealogies. The features of spectrum of aggregation of cancer in these families were a base of classification of family cancer of female reproductive organs. The analysis revealed 6 typical family situations. 2 of 6 syndromes are organ-specific (they show up as a cancer of the same localization, and 4 syndromes are variants of "general family cancer syndrome" and are characterized with wide spectrum of tumors mainly of the female reproductive organs.

Classification of variants of accumulation of cancer in Chernivtsi region:

1. Family ovarian cancer
2. Family endometrial cancer
3. Family ovarian and breast cancer
4. Family ovarian/endometrial and breast cancer
5. Family ovarian/endometrial/breast/colon cancer (Lynch II)
6. Family endometrial/gut cancer.

**Conclusions:** The results of the study could be a base for development and planning of early diagnostics and prevention of tumors in families of patients, such as the use of tumor markers, determination of genes of disposition, which is effective from the economic and social point of view.

## P6

### Generation of Coronavirus-based multigene RNA vectors

D. Makia, K.K. Eriksson, L. Cervantes, V. Thiel, B. Ludewig.  
*LFA, Research Department, St. Gallen, Switzerland*

Coronavirus-based vectors are currently considered a promising means to genetically deliver multiple heterologous genes to specific target cells. They are positive-stranded RNA viruses replicating in the cytoplasm without a DNA intermediary, making insertion of viral derived sequences into the host cell genome unlikely. Coronaviruses have the largest known RNA genome, therefore a cloning capacity of more than 6 kb is expected. They possess a unique transcription strategy resulting in the synthesis of 6-8 subgenomic mRNAs encoding mainly structural genes encoded at the 3' third of the genome, these genes can be replaced by multiple heterologous genes such as tumor antigens and cytokines. These vectors are attenuated since 2-3 structural genes are replaced resulting in replication competent

but propagation deficient vectors. An important consideration for viral vaccine vectors is the potential for efficient delivery of their genetic material to specific target cells. Targeting of viral vaccine vectors to dendritic cells (DCs) is highly desirable in order to optimise vaccine efficacy. The mouse hepatitis virus (MHV) and the human coronavirus (HCoV) 229E have their receptors (CEACAM-1 and hAPN or CD13, respectively) expressed on DCs and macrophages. This indicates that MHV and HCoV 229E based vectors could be used to deliver genetic cargo efficiently to DCs via receptor-mediated transduction. Since MHV is able to infect DCs, recombinant MHV vectors in the context of a murine model can serve as a paradigm for the development and evaluation of coronavirus vaccine vectors suitable for in vitro and in vivo transduction of human DCs. The anticipated results in the murine animal model will guide the development of coronavirus-based vaccines in general and will pave the way for the generation of HCoV 229E-based vaccines in humans.

## P7

### Immune surveillance-related genes are significantly over expressed in the breast epithelium of postmenopausal parous women

G.A. Balogh<sup>1</sup>, I.H. Russo<sup>1</sup>, C. Spittle<sup>2</sup>, R.C. Heulings<sup>1</sup>, D.A. Mailo<sup>1</sup>, J. Russo<sup>1</sup>. <sup>1</sup>*Fox Chase Cancer Center, Breast Cancer Research Laboratory, Philadelphia, United States of America;* <sup>2</sup>*Fox Chase Cancer Center, Biomarker and Genotyping Facility, Philadelphia, United States of America*

Endocrine and reproductive influences significantly affect play major roles in the lifetime risk steadily increasing incidence of breast cancer development in women. Nulliparity is one of the most firmly established risk factors for breast cancer, whereas early full term pregnancy and parity confer a significant protection. In order to elucidate the molecular pathways through which pregnancy exerts a protective effect, we have analyzed the genomic profile of lobules type 1 (Lob 1) present in reduction mammoplasty specimens obtained from 5 parous and 2 nulliparous postmenopausal women. Total RNA was obtained from epithelial cells of Lob 1 that were dissected using laser capture microdissection. RNAs were individually amplified employing oligo-DT T7 primer and in vitro transcription reaction. We hybridize cDNA microarrays containing 40,000 genes and after normalization of the data using Lowess method, we performed the confidence analysis of 99% level using GeneSight software. We found an interesting cluster of genes up-modulated ( $>2.0$  log,  $p < 0.01$ ) that were related to the immune system. In the present work we performed real time RT-PCR using a microfluidic card platform. The TaqMan<sup>®</sup> Low Density Immune Profiling Array contained 90 genes related to the immune system, and 18S rRNA as an internal control (Applied Biosystems 7900HT TaqMan<sup>®</sup> Low Density Array Upgrade, ABI). Epithelial cells from parous women significantly over-expressed 20 genes related to immune surveillance when compared with the RNA from nulliparous women. Those genes included: BCL2-associated X protein (BAX), complement component 3 (C3), chemokine (C-C motif), receptor 4 (CXCR4), CD34 antigen, Collagen IV (COL4A5), glucuronidase beta (GUSB), interleukin 1 b (IL-1b), interleukin 6 (IL6), major histocompatibility complex class II, DR alpha (HLA-DRA),